=> d his

(FILE 'HOME' ENTERED AT 16:25:13 ON 10 MAR 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 16:26:02 ON 10 MAR 2004

L1 919 S CD39
L2 8426 S INTRACEREBRAL(W)HEMORRHAGE
L3 1 S L1(7A)L2
L4 36659 S ADENOSINE(3A)DIPHOSPHATE OR ADPASE OR ATPDASE
L5 159 S L1(S)L4
L6 763 S (INCREAS? OR ENHANC?)(6A)L4
L7 1 S L1(8A)L6

=> d bib ab l3

L3 ANSWER 1 OF 1 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
AN 2003:315038 SCISEARCH
GA The Genuine Article (R) Number: 662VW
TI Metabolic control of excessive extracellular nucleotide accumulation by CD39/ecto-nucleotidase-1: Implications for ischemic vascular diseases
AU Marcus A J (Reprint); Broekman M J; Drosopoulos J H F; Islam N; Pinsky D J; Sesti C; Levi R
CS Columbia Univ, Coll Phys & Surg, Div Cardiol, Vet Affairs New York Harbor Healthcare Syst, 423 E 23rd St, New York, NY 10010 USA (Reprint); Columbia Univ, Coll Phys & Surg, Div Cardiol, Vet Affairs New York Harbor Healthcare Syst, New York, NY 10010 USA; Columbia Univ, Coll Phys & Surg, Dept Med, New York, NY 10010 USA; Cornell Univ, Weill Med Coll, Med Serv Hematol Oncol, Dept Med, New York, NY USA; Cornell Univ, Weill Med Coll, Med Serv Hematol Oncol, Dept Pathol, New York, NY USA; Cornell Univ, Weill Med Coll, Med Serv Hematol Oncol, Dept Pharmacol, New York, NY USA
CYA USA
SO JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (APR 2003) Vol. 305, No. 1, pp. 9-16.
Publisher: AMER SOC PHARMACOLOGY EXPERIMENTAL THERAPEUTICS, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998 USA.
ISSN: 0022-3565.
DT Article; Journal
LA English
REC Reference Count: 47
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Platelets are responsible for maintaining vascular integrity. In thrombocytopenic states, vascular permeability and fragility increase, presumably due to the absence of this platelet function. Chemical or physical injury to a blood vessel induces platelet activation and platelet recruitment. This is beneficial for the arrest of bleeding (hemostasis), but when an atherosclerotic plaque is ulcerated or fissured, it becomes an agonist for vascular occlusion (thrombosis). Experiments in the late 1980s cumulatively indicated that endothelial cell CD39 - an ecto-ADPase - reduced platelet reactivity to most agonists, even in the absence of prostacyclin or nitric oxide. As discussed herein, CD39 rapidly and preferentially metabolizes ATP and ADP released from activated platelets to AMP, thereby drastically reducing or even abolishing platelet aggregation and recruitment. Since ADP is the final common agonist for platelet recruitment and thrombus formation, this finding highlights the significance of CD39. A recombinant, soluble form of human CD39, solCD39, has enzymatic and biological properties identical to the full-length form of the molecule and strongly inhibits human platelet aggregation induced by ADP, collagen, arachidonate, or TRAP (thrombin receptor agonist peptide). In sympathetic nerve endings isolated from guinea pig hearts, where neuronal ATP enhances norepinephrine exocytosis, solCD39 markedly attenuated norepinephrine release. This suggests that NTPDase (nucleoside triphosphate diphosphohydrolase) could exert a cardioprotective action by

reducing ATP-mediated norepinephrine release, thereby offering a novel therapeutic approach to myocardial ischemia and its consequences. In a murine model of stroke, driven by excessive platelet recruitment, solCD39 reduced the sequelae of stroke, without an increase in **intracerebral hemorrhage**. **CD39** null mice, generated by deletion of apyrase-conserved regions 2 to 4, exhibited a decrease in postischemic perfusion and an increase in cerebral infarct volume when compared with controls. "Reconstitution" of CD39 null mice with solCD39 reversed these changes. We hypothesize that solCD39 has potential as a novel therapeutic agent for thrombotic diatheses.

=> d bib ab l7

L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:136929 CAPLUS
DN 134:173037
TI Method using CD39/ecto-ADPase for treating thrombotic and ischemic disorders
IN Pinsky, David J.
PA The Trustees of Columbia University in the City of New York, USA
SO PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001011949	A1	20010222	WO 2000-US22060	20000811
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002138858	A1	20020926	US 1999-374586	19990813
PRAI	US 1999-374586	A2	19990813		

AB The present invention provides a method of treating or preventing thrombotic or ischemic disorders in a subject which comprises administering an CD39/ecto-ADPase to the subject, wherein the **CD39** /ecto-**ADPase** inhibits ADP-mediated platelet aggregation by **increasing** ADP catabolism, and a method for determining whether a compound inhibits platelet aggregation by increasing ADP catabolism so as to treat or prevent thrombotic or ischemic disorders in a subject, comprising: (a) inducing thrombotic or ischemic disorders in an animal, which animal is an animal model for thrombotic or ischemic disorders; (b) measuring the stroke outcome in said animal; (c) measuring platelet deposition and/or fibrin deposition in ischemic tissue; and (d) comparing the stroke outcome in step (b) and the platelet deposition and/or fibrin deposition with that of the animal model in the absence of the compound so as to identify a compound capable of treating or preventing thrombotic or ischemic disorders in a subject. Also disclosed are human CD39/ecto-ADPase sequences.
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> d his

(FILE 'HOME' ENTERED AT 17:42:22 ON 10 MAR 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 17:44:10 ON 10 MAR 2004

L1 4594 S CD39 OR ECTO-ADPASE OR APYRASE
L2 17548 S (TREAT? OR PREVENT?)(4A)STROKE
L3 2 S L1(8A)L2
L4 2 DUP REM L3 (0 DUPLICATES REMOVED)

=> d bib ab 1-2 l4

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:262463 CAPLUS
DN 139:206845
TI Metabolic control of excessive extracellular nucleotide accumulation by CD39/ecto-nucleotidase-1: Implications for ischemic vascular diseases
AU Marcus, Aaron J.; Broekman, M. Johan; Drosopoulos, Joan H. F.; Islam, Naziba; Pinsky, David J.; Sesti, Casilde; Levi, Roberto
CS Department of Medicine, Weill Medical College of Cornell University, New York, NY, USA
SO Journal of Pharmacology and Experimental Therapeutics (2003), 305(1), 9-16
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal; General Review
LA English
AB A review. Platelets are responsible for maintaining vascular integrity. In thrombocytopenic states, vascular permeability and fragility increase, presumably due to the absence of this platelet function. Chemical or phys. injury to a blood vessel induces platelet activation and platelet recruitment. This is beneficial for the arrest of bleeding (hemostasis), but when an atherosclerotic plaque is ulcerated or fissured, it becomes an agonist for vascular occlusion (thrombosis). Expts. in the late 1980s cumulatively indicated that endothelial cell CD39-an ecto-ADPase-reduced platelet reactivity to most agonists, even in the absence of prostacyclin or nitric oxide. As discussed herein, CD39 rapidly and preferentially metabolizes ATP and ADP released from activated platelets to AMP, thereby drastically reducing or even abolishing platelet aggregation and recruitment. Since ADP is the final common agonist for platelet recruitment and thrombus formation, this finding highlights the significance of CD39. A recombinant, soluble form of human CD39, solCD39, has enzymic and biol. properties identical to the full-length form of the mol. and strongly inhibits human platelet aggregation induced by ADP, collagen, arachidonate, or TRAP (thrombin receptor agonist peptide). In sympathetic nerve endings isolated from guinea pig hearts, where neuronal ATP enhances norepinephrine exocytosis, solCD39 markedly attenuated norepinephrine release. This suggests that NTPDase (nucleoside triphosphate diphosphohydrolase) could exert a cardioprotective action by reducing ATP-mediated norepinephrine release, thereby offering a novel therapeutic approach to myocardial ischemia and its consequences. In a murine model of stroke, driven by excessive platelet recruitment, solCD39 reduced the sequelae of stroke, without an increase in intracerebral hemorrhage. CD39 null mice, generated by deletion of apyrase-conserved regions 2 to 4, exhibited a decrease in postischemic perfusion and an increase in cerebral infarct volume when compared with controls. "Reconstitution" of CD39 null mice with solCD39 reversed these changes. We hypothesize that solCD39 has potential as a novel therapeutic agent for thrombotic diatheses.
RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:486846 CAPLUS
DN 139:190447
TI New antiplatelet strategies in stroke prevention and treatment
AU Weksler, Babette B.; Pena-Alvarez, Jose
CS Division of Hematology-Oncology at Weill Medical College, Cornell University, Ithaca, NY, USA
SO Drug Therapy for Stroke Prevention (2001), 94-110. Editor(s): Bogousslavsky, Julien. Publisher: Taylor & Francis Ltd., London, UK. CODEN: 69EDI6; ISBN: 0-7484-0934-3
DT Conference; General Review
LA English
AB A review. A continued search for more effective antiplatelet therapy appears important for improving the prevention and treatment of occlusive stroke, since current therapies are of limited benefit compared with efficacy of antiplatelet approaches to acute cardiac events. Measures that decrease the classic risk factors for cerebral ischemia, which often involve increased platelet reactivity, form the backbone of preventive strategies. While aspirin remains the best agent for patients who have had previous TIA and stroke, its benefits are modest (<25 % risk reduction in secondary prevention and about 12 % risk reduction in acute stroke) and combining aspirin with other known antithrombotics may well elevate risk of intracranial hemorrhage. Truly new approaches remain in the preclin. stage overall at the present time. Usage of platelet GPIIbIIIa antagonists is effective in reducing stroke damage in many animal models but has not yet been examined in clin. trials of stroke, in part because of concern about bleeding risk. Measures to block iNOS and to utilize NO donors to enhance endothelial NO production have also been shown to prevent brain damage and improve cerebral blood flow after exptl. cerebral ischemia; techniques to target N0-interventional strategies to areas of vascular damage are being developed. The soluble, recombinant form of the endothelial ectoADPase, CD39, which has antiplatelet effects in vitro, has been used in a mouse model of acute stroke where its infusion shows promising efficacy in reducing infarct size and restoring cerebral blood flow without incurring hemorrhage. Further development and clin. application of such novel measures are awaited with great interest.
RE.CNT 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L6	seo adj id near3 2	103	L6

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L5	l1 and L4	0	L5
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L3	l1 and L2	0	L3
L2	cd39	113	L2
L1	6548520.pn.	1	L1

END OF SEARCH HISTORY

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